REMARKS

Claims 1, 3, 4, 9, 11, 14, 23, 25, and 33 have been amended. The claims presently examined include claims 1-6, 9-18, 21-28, and 33. Applicants respectfully request allowance of those examined claims.

Objections to the Specification

The Examiner objected to the title as allegedly not being descriptive because the elected inventions are directed to a method, system, and computer readable medium instead of methods, systems, and articles of manufacture. Action at page 2, item 3. The title has been amended to recite "METHODS, SYSTEMS, AND COMPUTER READABLE MEDIUMS FOR EVALUATING BIOLOGICAL DATA."

The Examiner objected to the blank space at page 10, line 10. Action at page 2, item 4. Applicants amend page 10 of the specification to include the appropriate PCT publication number in place of the blank line.

The Examiner objected to the specification because it includes two different tables that are designated as "Table 5." Action at page 2, item 5. Applicants amend the specification to remove "TABLE 5" from page 91, and have moved that information in the application as a figure.

The Examiner objected to the table on page 87 and flow chart on page 91, and stated that they need to be in the form of formal drawings. Action at page 2, item 6. Applicants submit a new Figure 47, which incorporates the flow chart on page 91 of the original specification. Applicants assert, however, that tables in the specification are acceptable. Thus, the table at page 87 is proper and need not be in the form of a formal drawing.

Amendments to the Drawings

The attached sheet of drawing includes a new Figure 47. Applicants request approval of new Figure 47 in the accompanying Request to Approve New Drawing. Attachment: New Sheet (one sheet, new Figure 47).

Accordingly, Applicants request the Examiner to withdraw the objections to the specification.

Rejection Under 35 U.S.C. § 112, ¶ 2

The Examiner rejected claims 1-6 and 9-13 under 35 U.S.C. § 112, second paragraph, for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Action at page 3, item 8.

Specifically, regarding claims 1, 3, 4, and 9, the Examiner indicates that "nowhere in the actual claim steps is the computer implementation required which causes the claims to be vague and indefinite." Action at page 3, item 9. Applicants respectfully submit that one of skill in the art would know that the methods recited in those claims are to be performed by a computer in view of the preambles of the claims. Therefore, those claims are definite and clear. Solely in an effort to expedite prosecution and not acquiescing to the rejection, claims 1, 3, 4, and 9 have been amended to recite "using a computer, ..." Accordingly, this basis for the rejection is moot.

The Examiner also contends that claims 1 and 11 lack sufficient antecedent basis for the language "the results of each algorithm." Solely to expedite prosecution and not acquiescing to the rejection, applicants amended claims 1 and 11 to recite "depending on agreement between the results of at least two of the algorithms . . . ." In view of the prior language in the claims that recites "applying at least two different allele calling algorithms to the data to provide a result for each algorithm," there is antecedent basis for the language "depending on agreement between the results of at least two of the algorithms . . . ." Accordingly, applicants request the Examiner to withdraw this basis for the section 112, second paragraph, rejection of claims.

Rejection Under 35 U.S.C. § 101

The Examiner rejected claims 1-6, 9-18, 21-28, and 33 under 35 U.S.C. § 101 for allegedly being directed to non-statutory algorithm type subject matter. Action at page 4, item 13. The Examiner asserted that a physical alteration step of data is a requirement in determining non-statutory subject matter. Action at page 4, item 14. Applicants respectfully traverse this rejection.

The Examiner cites no law to support the contention that a physical alteration step outside the system or computer is required for statutory subject matter. See Action at page 4, items 14 to 16. In fact, the MPEP and the law do not require a physical alteration step outside the system or computer. Instead, if the claimed invention as a whole produces a "useful, concrete, and tangible result," the invention is directed to statutory subject matter. *See* MPEP § 2106 II(A) and § 2106 IV(B)(2)(b)(ii), citing to *State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 149 F.3d 1368, 1374 (Fed. Cir. 1998). The claimed invention here allows one to identify or make an allele call. That is clearly a "useful, concrete, and tangible result."

Also, the Examiner provides an example from the MPEP as follows: "For example, a computer process that simply calculates a mathematical algorithm that models noise is nonstatutory. However, a claimed process for digitally filtering noise employing the mathematical algorithm is statutory." Action at page 4, item 14. The Examiner contends that the claimed invention in this case is similar to the simple calculation of the mathematical algorithm that models noise. Applicants respectfully disagree. In the present claims, the allele calling algorithms are used to identify or make an allele call. That is not simple algorithmic modeling. Rather, the useful and tangible result of identifying or making an allele call is accomplished.

Therefore, Applicants respectfully request withdrawal of the § 101 rejection.

Rejection Under 35 U.S.C. § 102(a)

The Examiner rejected claims 1-6, 9-18, 21-28, and 33 under 35 U.S.C. § 102(a)

as allegedly being anticipated by Allex et al., Neural Network Representations Input That

Produce Accurate Consensus Sequences From DNA Fragment Assemblies, Bioinformatics, Vol.

15, No. 9, pp. 723-728 (1999) (Allex). Action at page 5, item 2. The Examiner contends that

Allex "discloses a method of using a system for consensus calling by processing fluorescent

trace data . . . . The system of [Allex] accepts fluorescent trace data as inputs . . . wherein base

calls area indicated by total agreement (Figure 1), as in instant claim 1, line 2." Action at page 5,

items 3 and 4. The Examiner also contends that the method of Allex comprises five network

topologies. Applicants respectfully traverse the rejection.

Applicants first address independent claims 1, 9, 11, 21, 23, and 33, and the claims that

depend from those claims. Each of independent claims 1, 9, 11, 21, 23, and 33 include applying

at least two different allele calling algorithms to data, and using the results of at least two of the

algorithms to make or identify a call and/or assign a confidence level to a call.

At the outset, applicants note that Allex uses the term "consensus" to describe the

sequence resulting from the comparison of different individually sequenced samples. A

"consensus sequence" is "[t]he nucleotides or amino acids most commonly found at each

position in the sequences of related DNAs, RNAs, or proteins." Molecular Cell Biology, Lodish

et al., W.H. Freeman and Company, page G-4, 2000. Consequently, consensus calling in Allex

refers to a method of determining a consensus sequence and does not suggest using a consensus

of more than one calling algorithm to determine such a sequence.

In fact, Allex discusses separately using five neural networks to determine a consensus sequence from multiple samples of DNA. See, e.g., Allex at the Discussion section at pages 727 to 728 and Figure 10. Allex compares the effectiveness of each of the networks used separately. Nowhere, however, does Allex suggest combining any of the five neural networks in a manner in which separate results from more than one of the networks are used to make a call. Thus, in contrast to the presently claimed invention in independent claims 1, 9, 11, 21, 23, and 33, Allex does not disclose applying at least two different allele calling algorithms to data, and using the results of at least two of the algorithms to make a call and/or assign a confidence level to a call. Accordingly, for at least this reason, Allex fails to show every element of independent claims 1, 9, 11, 21, 23, and 33, and the claims that ultimately depend from those claims (claims 2, 6, 10, 12, 13, 22, 24, and 28). Thus, Allex fails to anticipate those claims.

Next, independent claim 3 is directed to a computer-implemented method for making allele calls, comprising: receiving a signal representing nucleic acid information; using a computer, analyzing the signal to determine if the signal meets a threshold test of an allele caller making a correct call, and making an allele call for the signal if the threshold test is met. Independent claim 14 is directed to a system for making allele calls, comprising, among other elements, a memory containing program instructions for execution by the processor to receive a signal representing nucleic acid information, analyze the signal to determine if the signal meets a threshold test of an allele caller making a correct call, and make an allele call for the signal if the threshold test is met. Independent claim 25 is directed to a computer readable medium containing instructions for controlling a computer system to perform a method for making allele calls, the method comprising: receiving a signal representing nucleic acid information;

analyzing the signal to determine if the signal meets a threshold test of an allele caller making a correct call, and making an allele call for the signal if the threshold test is met.

The Examiner contends that Allex discusses making ambiguous calls "by setting a threshold, if more than one output exceeds the threshold (defined complexity), then the appropriate ambiguous call is made." Action at page 6, item 7. "If only one output is above the threshold (predefined complexity), the call is unambiguous . . . . Therefore, the call is determined for outputs exceeding a threshold and no calls are determined for the outputs below said threshold (predefined complexity), as in instant claim 3." Action at page 6, item 7. The Examiner makes a similar statement concerning claim 25. Action at page 7, item 12.

Applicants respectfully assert that the discussion of a threshold in Allex does not suggest analyzing the signal to determine if the signal meets a threshold test of an allele caller making a correct call, and making an allele call for the signal if the threshold test is met. Rather, Allex makes a call irrespective of whether or not the value exceeds a threshold. The threshold is used to determine which call is made, not whether or not a call is made at all. Specifically, Allex states

> [a]mbiguous calls may also be made by setting a threshold. If more than one output exceeds the threshold, then the appropriate ambiguous call is made. If only one output is above the threshold, the call is unambiguous." In non-heterozygote DNA sequences, human editors resolve ambiguous calls to one of the four bases before submission to GenBank. Ambiguous calls serve to focus editors' attention on areas in the consensus that warrant closer examination. In the case of heterozygote genomes, ambiguous calls pinpoint differences between the alleles.

Allex at page 726, paragraph bridging first and second columns.

Allex does not discuss an option of not making a call at all based on a failure to meet a threshold test of an allele caller making a correct call. Thus, for at least this reason Allex fails to show every element of independent claims 3, 14, and 25, and the

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claims that ultimately depend from those claims (claims 6, 15, and 28). Accordingly, Allex fails to anticipate those claims.

Next, independent claim 4 is directed to a computer-implemented method for making allele calls, comprising: receiving a signal representing nucleic acid information; using a computer, applying a set of filters to the signal to eliminate peaks that do not represent alleles, wherein the set of filters include at least one of the following: [a list of checkers]; and determining the remaining peaks in the data are alleles after applying the set of filters to the signal. Independent claim 16 is directed to a system for making allele calls, comprising, among other elements, a memory containing program instructions for execution by the processor to receive a signal representing nucleic acid information, apply a set of filters to the signal to eliminate peaks that do not represent alleles, wherein the set of filters include at least one of the following [a list of checkers], and determine the remaining peaks in the data are alleles after applying the set of filters to the signal. Independent claim 26 is directed to a computer readable medium containing instructions for controlling a computer system to perform a method for making allele calls, the method comprising: receiving a signal representing nucleic acid information; applying a set of filters to the signal to eliminate peaks that do not represent alleles, wherein the set of filters include at least one of the following: [a list of checkers]; and determining the remaining peaks in the data are alleles after applying the set of filters to the signal.

Addressing claims 4, 16, and 26, the Examiner contends that Allex discusses "[t]he base calls and traces conflict and the appropriate code is listed as the consensus call...a base calls that have been erroneously inserted, the consensus show as gap, meaning no base exists (filter)

(Figure 1). Trace peaks are evaluated a medium shoulder is associated with zero slope (Figure 3) . . . ." Action at page 6, item 8.

Applicants respectfully assert that the discussion in Allex cited by the Examiner fails to anticipate independent claims 4, 16, and 26. First, Figure 1 in Allex shows a comparison of sequences already determined to obtain a consensus sequence. The first two highlighted columns show where there is variation between bases of certain separate sequences already determined. In view of the variation, an ambiguity code is listed for the consensus call. In the third highlighted column, a conclusion is made that an erroneously inserted base exists in the sequence determined for the first fragment in view of the absence of such a base in the sequences determined for other fragments.

In contrast to claims 4, 16, and 26, Figure 1 fails to show applying a set of filters to the signal to eliminate peaks that do not represent alleles . . . . and determining that remaining peaks in the data are alleles after applying the set of filters to the signal. Rather, Figure 1 compares separate sequences that have already been determined to obtain a consensus sequence. That discussion does not show or suggest eliminating peaks in a process of sequencing by applying a set of filters to a signal.

Second, Figure 3 also fails to show claims 4, 16, and 26. Specifically, Figure 3 discusses classifications of peak shapes and intensity. Figure 7 discusses the use of the peak classifications. The peak classifications are inputted into the neural network that is used for sequencing in order to determine the sequence. In contrast to claims 4, 16, and 26, that discussion fails to show applying a set of filters to the signal to eliminate peaks that do not represent alleles . . . . and determining that remaining peaks in the data are alleles after applying the set of filters to the signal. Rather, the information is used to determine a base in a sequence,

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and it is not an elimination of peaks that do not represent alleles by applying a set of filters, and a determination that remaining peaks that are not eliminated are alleles.

Thus, for at least this reason Allex fails to show every element of independent claims 4, 16, and 26, and the claims that ultimately depend from those claims (claims 5, 6, 17, 18, and 28). Accordingly, Allex fails to anticipate those claims.

Applicants respectfully request reconsideration and withdrawal of the section 102(a) rejection.

Conclusion

Applicants request the Examiner's reconsideration and reexamination of the application, and the timely allowance of the pending claims. If the Examiner does not agree that the application is in condition for allowance, Applicants request the Examiner to call the undersigned at 650-849-6620 to schedule an interview.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

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Dated: September 28, 2004   By:_____

M. Paul Barker
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